DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
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Siemens Healthcare Diagnostics Inc.
c/o Ms. Sara Kastrup
Regulatory Clinical Affairs Specialist
511 Benedict Avenue
Tarrytown, NY 10591

January 23, 2015

Re: k143352
Trade/Device Name: IMMULITE® 2000 Ferritin Calibration Verification Material (CVM)
IMMULITE® 2000 IGFBP-3 Calibration Verification Material (CVM)
Regulation Number: 21 §CFR 862.1660
Regulation Name: Quality Control Material (assayed and unassayed)
Regulatory Class: Class I, Reserved
Product Code: JJX
Dated: November 21, 2014
Received: November 24, 2014

Dear Ms. Kastrup:

This letter corrects our substantially equivalent letter of December 24, 2014.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must

comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Elizabeth A. Stafford -S

for Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k143352

Device Name
IMMULITE® 2000 Ferritin Calibration Verification Material (CVM)
IMMULITE® 2000 IGFBP-3 Calibration Verification Material (CVM)

Indications for Use *(Describe)*
The IMMULITE® Ferritin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Ferritin assay on the IMMULITE 2000 systems
The IMMULITE® IGFBP-3 Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE IGFBP-3 assay on the IMMULITE 2000 systems

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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SIEMENS

510(k) Summary

510(k) Summary – IMMULITE 2000 Ferritin Calibration Master Verification Material

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: k143352

1. Submitter:	
Mailing Address:	Siemens Healthcare Diagnostics Inc. 511 Benedict Avenue Tarrytown, NY 10591
Contact Person:	Sara Kastrup Regulatory Clinical Affairs Specialist
Phone Number:	(914)-524-2317
Fax Number:	(914)-524-2101
E-mail Address:	sara.kastrup@siemens.com
Date Prepared:	December 23, 2014
2. Device Name:	
Proprietary Name:	**IMMULITE® 2000 Ferritin Calibration Verification Material**
Measurand:	Quality Control materials for IMMULITE® 2000 Ferritin assay
Type of Test:	Calibration Verification Material (CVM) for IMMULITE® 2000 Ferritin assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Clinical Chemistry (75)
3. Predicate Device Name:	IMMULITE® 2000 HCG Calibration Verification Material (CVM)
Predicate 510(k) No:	k133128
4. Device Description:	The Ferritin Calibration Verification Material (CVM) contains one set of four vials. CVM1 contains 5.0mL of human serum albumin with preservatives. CVM2, CVM3, and CVM4 contain 2.0mL/vial of various levels of human ferritin in a human serum albumin matrix with preservatives. The CVMs are supplied in liquid form.

5. Intended Use: **Indication for Use:**	See Indications for Use Statement below: The IMMULITE® Ferritin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Ferritin assay on the IMMULITE 2000 systems.
Special Conditions for Use Statement(s):	For prescription use only
Special Instrument Requirements:	IMMULITE® 2000 Systems
6. Technological Characteristics and Substantial Equivalence Comparison with Predicate:	A comparison of the device features, intended use, and other information demonstrates that the IMMULITE® 2000 Ferritin Calibration Verification Material (CVM) is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: Substantial Equivalence Comparison

SIMILARITIES		
	Candidate Device IMMULITE 2000 Ferritin CVM	**Predicate Device IMMULITE 2000 HCG CVM**
Intended Use	The IMMULITE® Ferritin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Ferritin assay on the IMMULITE 2000 systems.	The IMMULITE® HCG Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE HCG assay on the IMMULITE 2000 systems.
Form	Liquid	Same
Stability	Stable unopened until the expiration date	Same
Levels	4	Same
Use	Single Use Only	Same

	DIFFERENCES	
	Candidate Device IMMULITE 2000 Ferritin CVM	**Predicate Device IMMULITE 2000 HCG CVM**
Analyte	Ferritin	HCG
Storage	2 -8 ^{o}C	-20°C
Matrix	Human Serum Albumin with Preservatives	Human Serum with Preservatives

7. Non-Clinical Performance Testing

Performance testing has been carried out to demonstrate that this device meets the performance specifications for its intended use. The following tests were performed on the candidate device.

7.1 Stability Summary:

The stability study was conducted to validate real-time shelf life and open component (in-use or open vial) claim for the IMMULITE 2000 Ferritin Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM before and after reconstitution.

The IMMULITE® 2000 Ferritin Calibration Verification Materials: The Calibration Verification Materials are stable up to 18 months when stored at 2-8°C prior to opening and for 8 hours at ambient or room temperature (15-25°C) after reconstitution.

7.1.1 Stability Protocol Summary:

The CVM study protocols are run as part of the calibrator stability testing. The stability CVMs and reference CVMs are run in duplicate (as a minimum) at the time points shown in **Table 2** and the dose value determined from the reference calibrator curve.

Table 2: Stability Time Points

CVM level	Time-Points (months)			
LFECVM1	0	6	12	18
LFECVM2	0	6	12	18
LFECVM3	0	6	12	18
LFECVM4	0	6	12	18

For Open Component testing, the results are determined from a 2-point adjustment. Using IMMULITE 2000 Ferritin (L2KFE2) kit lot 327, Ferritin CVM lot 016A was tested at 2-hourly intervals for up to 9 hours at ambient or room temperature (15-25°C) conditions and compared to the determinations at time zero.

7.1.2 Stability Acceptance Criteria Summary:

The Acceptance Criteria for the IMMULITE Ferritin requires dose value of stability calibrator/CVM to fall between ±14% of assigned dose for CVM level 2, ±8% for CVM level 3 and 15% for CVM level 4. The sponsor's acceptance criteria are summarized in **Table 3**.

Table 3 Acceptance criteria for stability of IMMULITE 2000 Ferritin CVM

CVM level	Assigned Dose (ng/mL)	Guideline Criteria % difference to assigned dose	Acceptable dose range (ng/mL)
LFECVM1	0.00	Not Applicable	1.5
LFECVM2	16.2	±14%	13.9-18.5
LFECVM3	241	±8%	222-260
LFECVM4	1909	±15%	1623-2195

7.2 Traceability:

The IMMULITE Ferritin is traceable to WHO 2nd IS 80/578. The CVMs are manufactured using qualified materials and measurement procedures.

7.3 Value Assignment:

IMMULITE Ferritin CVMs are 4 level materials which are a subset of 10 level Ferritin calibrators. Calibrators are not commercialized but are used internally during manufacture and release testing of Ferritin reagents and two point adjustors.

The IMMULITE calibrators and therefore CVMs are value assigned using assigned reference calibrators. The assigned reference calibrators are prepared using Ferritin antigen stock and are traceable to WHO 2nd IS 80/578. Five levels of commercially available controls and 30 samples (15 spiked and 15 normal samples were used to validate calibrator/CVM value assignments.

The CVMs are manufactured using qualified materials and measurement procedures. The IMMULITE Ferritin calibrators/CVMs were tested on 4 different days, on 15 replicates in total, comprised of 5 runs, 3 replicates per run, 5 IMMULITE 2000 systems and 3 different reagent kit lots. The CVMs dose values are generated using curve generated by assigned reference calibrators. The CVM values are calculated based on the recovered values for each run on each instrument independently. CVM values are then averaged across all systems. Quality control is performed by calculating the recovery of patient samples and controls using the assigned CVM values. The controls must fall within their target ranges.

7.4 Expected Values/Reference Range:

Each CVM level was tested on tested on 4 different days, on 15 replicates in total, comprised of 5 runs, 3 replicates per run, 5 IMMULITE 2000 systems and 3 different reagent kit lots. The Guideline Range (95% confidence interval) for each CVM level was established based on the Target Mean and ± 2 Standard Deviation (SD). The expected values are provided in the IMMULITE® 2000 CVM Calibration Verification Material lot-specific package insert.

The expected assay range is up to 1500 ng/mL. The target values in **Table 4** can be considered as guidelines; each lot will have lot-specific values.

Table 4: Target Values

Analyte target levels	**CVM Level**	**Target Mean (ng/mL)**	**Standard Deviation (SD)**	**Guideline ±2SD Range (ng/mL)**	
	LFECVM1	0.00	-	0.00	1.50
	LFECVM2	16.2	1.15	13.9	18.5
	LFECVM3	246	13.5	219	273
	LFECVM4	2051	-	-	-
	75% LFECVM4+ 25% LFECVM1	1538	115.5	1307	1769
Assay Range	Up to 1500 ng/mL				

Each laboratory should establish their limits for acceptability based on methodology, clinical significance and medical decision levels of the test analyte. The representative, total precision tabulated in the respective assay instructions for use may be considered as one factor when establishing local, acceptable ranges. The values provided above may be considered as guidelines. Value assignment is lot-specific.

7.5 Standard/Guidance Documents Referenced**:**

- CEN 13640 Stability Testing of In Vitro Diagnostic Reagents
- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

7.6 Proposed Labeling**:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10

8. Conclusion:

The IMMULITE® 2000 Ferritin Calibration Verification Material is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the FDA cleared IMMULITE® 2000 HCG Calibration Verification Material. The substantial equivalence of the device is supported by the non-clinical testing and was found to be comparable and supports the claims of substantial equivalence, product safety and effectiveness. Based on the testing completed and the comparisons with predicate device, the IMMULITE® 2000 Ferritin Calibration Verification Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.

SIEMENS

510(k) Summary - IMMULITE 2000 IGFBP-3 Calibration Master Verification Material

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.
The assigned 510(k) Number: k143352

1. **Submitter:**

Mailing Address: Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591

Contact Person: Sara Kastrup
Regulatory Clinical Affairs Specialist
Phone Number: (914)-524-2317
Fax Number: (914)-524-2101
E-mail Address: sara.kastrup@siemens.com

Date Prepared: December 23, 2014

2. **Device Name:**

Proprietary Name: **IMMULITE® 2000 IGFBP-3 Calibration Verification Material**
Measurand: Quality Control material for IMMULITE® 2000 IGFBP-3 assay
Type of Test: Calibration Verification Material (CVM) for IMMULITE® 2000 IGFBP-3 assay
Regulation Section: 21 CFR 862.1660, Quality Control Material
Classification: Class I Reserved
Products Code: JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)

Panel: Clinical Chemistry (75)

3. **Predicate Device Name**
Predicate 510(k) No: IMMULITE® 2000 IGF-1 Calibration Verification Material (CVM)
K140818

4. **Device Description:** IMMULITE® 2000 IGFBP-3 Calibration Verification Material (CVM) contains one set of four vials each 2.0mL/vial . CVM1 contains bovine protein buffer matrix with preservatives. CVM2, CVM3 and CVM4 contain various levels of processed human serum (source of IGFBP-3) in bovine protein buffer matrix with preservatives. The CVMs are supplied in liquid form.

5. **Intended Use:** See Indications for Use Statement below

Indication for Use: The IMMULITE® IGFBP-3 Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE IGFBP-3 assay on the IMMULITE 2000 systems.

Special Conditions for Use Statement(s):	For prescription use only
Special Instrument Requirements:	IMMULITE® 2000 Systems
6. Technological Characteristics and Substantial Equivalence Comparison with Predicate:	A comparison of the device features, intended use, and other information demonstrates that the IMMULITE® IGFBP-3 Calibration Verification Material (CVM) is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: Substantial Equivalence Comparison

SIMILARITIES		
	Candidate Device IMMULITE 2000 IGFBP-3 CVM	**Predicate Device IMMULITE 2000 IGF-1 CVM**
Intended Use	The IMMULITE® IGFBP-3 Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE IGFBP-3 assay on the IMMULITE 2000 systems	The IMMULITE® IGF-1 Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE IGF-1 assay on the IMMULITE 2000 systems
Storage	-20°C	Same
Stability	Stable unopened until the expiration date	Same
Levels	4	Same
Use	Single Use Only	Same
Matrix	Bovine Protein with preservatives	Same
Form	Liquid	Same

DIFFERENCES		
	Candidate Device IGFBP-3 CVM	**Predicate Device IMMULITE 2000 IGF-1 CVM**
Analyte	IGFBP-3	IGF-1

7. Non-Clinical Performance Testing

Performance testing has been carried out to demonstrate that this device meets the performance specifications for its intended use. The following tests were performed on the candidate device.

7.1 Stability Summary:

The stability study was conducted to validate shelf life claim for the IMMULITE 2000 IGFBP-3 Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM before and after reconstitution.

The IGFBP-3 Calibration Verification Materials are stable up to 4 years when stored at -20°C.

7.1.1 Stability Protocol Summary:

The CVM study protocols are run as part of the calibrator stability testing. The stability CVMs and reference CVMs are run in duplicate (as a minimum) at the time points shown in **Table 2** and the dose value determined from the reference calibrator curve.

Table 2: Stability Time Points

CVM Level	Time-Points (months)			
LGBCVM1	0	30	36	48
LGBCVM2	0	30	36	48
LGBCVM3	0	30	36	48
LGBCVM4	0	30	36	48

7.1.2 Stability Acceptance Criteria Summary:

The sponsor's Acceptance Criteria for the IMMULITE IGFBP-3 criteria requires dose value of stability calibrator/CVM to fall between ±10% of assigned dose for CVM level 2 and level 3, and ±15% for CVM level 4.

The acceptance criteria are summarized in **Table 3**.

Table 3 Acceptance criteria for stability of IMMULITE 2000 IGFBP-3 CVM

CVM level	Assigned Dose (µg /mL)	Guideline Criteria % difference to assigned dose	Acceptable dose range (µg /mL)
LGBCVM1	**0.00**	**N/A**	**≤0.5**
LGBCVM2	**1.10**	**±10%**	**0.99-1.21**
LGBCVM3	**4.12**	**±10%**	**3.71-4.53**
LGBCVM4	**18.9**	**±15%**	**16.1-21.7**

7.2 Traceability:
The IMMULITE IGFBP-3 CVMs are traceable to WHO NIBSC Reagent 93/560. The CVMs are manufactured using qualified materials and measurement procedures.

7.3 Value Assignment:
The IGFBP-3 CVMs are 4 level materials are a subset of 8 level IGFBP-3 calibrators.
Calibrators are not commercialized but are used internally during manufacture and release testing of IGFBP-3 reagents and two point adjustors.

The IMMULITE calibrators and therefore CVMs are value assigned using assigned reference calibrators. The assigned reference calibrators are prepared using IGFBP-3 antigen stock and are traceable to WHO NIBSC Reagent 93/560. Two levels of commercially available controls and 30 diluted normal samples were used to validate calibrator/CVM value assignments.

The calibrators/CVMs are manufactured using qualified materials and measurement procedures. The calibrators/CVMs were tested on 3 different days, on 15 replicates in total, comprised of 5 runs, 3 replicates per run, 3 IMMULITE 2000 systems and 3 different reagent kit lots. The CVMs dose values are generated using curve generated by assigned reference calibrators. The CVM values are calculated based on the recovered values for each run on each instrument independently. CVM values are then averaged across all systems. Quality control is performed by calculating the recovery of patient samples, spiked patient samples and controls using the assigned CVM values. The controls must fall within their target ranges.

7.4 Expected Values/Reference Range:

Each CVM level was on 3 different days, on 15 replicates in total, comprised of 5 runs, 3 replicates per run, 3 IMMULITE 2000 systems and 3 different reagent kit lots. The Guideline Range (95% confidence interval) for each CVM level was established based on the Target Mean and ± 2 Standard Deviation (SD). The expected values are provided in the IMMULITE® 2000 IGFBP-3 CVM Calibration Verification Material lot-specific package insert.

The expected assay range is up to16 µg/mL. The target values in **Table 4** can be considered as guidelines; each lot will have lot-specific values.

Table 4: Target Values

Analyte target levels	**CVM Level**	**Target Mean (µg/mL)**	**Standard Deviation (SD)**	**Guideline ±2SD Range (µg/mL)**	
	LGBCVM1	0.00	-	0.00	0.5
	LGBCVM2	0.915	0.0575	0.80	1.03
	LGBCVM3	4.11	0.31	3.49	4.7
	LGBCVM4	17.8	-	-	-
	90% LGBCVM4 + 10% LGBCVM1	16.0	1.2	13.6	18.4
Assay Range	Up to 16 µg /mL				

Note: CVM4 requires dilution to ensure that the target value is within +10% of the top of the reportable range of the assay

Each laboratory should establish their limits for acceptability based on methodology, clinical significance and medical decision levels of the test analyte. The representative, total precision tabulated in the respective assay instructions for use may be considered as one factor when establishing local, acceptable ranges. The values provided above may be considered as guidelines. Value assignment is lot-specific.

7.5 Standard/Guidance Documents Referenced**:**

- CEN 13640 Stability Testing of In Vitro Diagnostic Reagents
- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

7.6 Proposed Labeling**:**
The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10

8. Conclusion:

The IMMULITE® 2000 IGFBP-3 Calibration Verification Material is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the FDA cleared IMMULITE® 2000 IGF-1 Calibration Verification Material. The substantial equivalence of the device is supported by the non-clinical testing and was found to be comparable and supports the claims of substantial equivalence, product safety and effectiveness. Based on the testing completed and the comparisons with predicate device, the IMMULITE® 2000 IGFBP-3 Calibration Verification Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.